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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,989	05/23/2000	Charles M. Rice III	6029-4356	1745

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EXAMINER

WORTMAN, DONNA C

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 12/03/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/576,989

Applicant(s)

RICE ET AL.

Examiner

Donna C. Wortman, Ph.D.

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1,3-24,29,41-44,61-70 and 72-75 is/are pending in the application.
- 4a) Of the above claim(s) 18-24,41-44 and 63-68 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-11,29,61,62,69,70 and 72-75 is/are rejected.
- 7) ☒ Claim(s) 12-17 is/are objected to.
- 8) ☒ Claim(s) 1,3-24,29,41-44,61-70 and 72-75 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13a + 14
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648.

Claims 1, 3-24, 29, 41-44, 61-70, and 72-75 are pending. Claims 1, 3-17, 29, 61, 62, 69, 70 and 72-75 are under examination.

Claims 18-24, 41-44, and 63-68 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Applicant has again argued that the restriction requirement, which was made final in Paper No. 9, is improper and has argued that if claim 1 is found to be patentable, all of the claims currently pending would necessarily be patentable.

These arguments have been considered but not found persuasive. Claims dependent from a patentable independent claim may or may not be patentable, since each claim must meet all statutory requirements in order to be patentable, and in fact may require additional consideration and separate search(es) as previously explained. Applicant has retained the right to petition from the requirement under 37 CFR 1.144. See MPEP § 818.03(c).

Claims 1, 12, 70 and 72 were amended in Paper No.13.

Applicant's remarks concerning priority and the effective filing date of this application have been considered but not found persuasive. The effective filing date of the instant claims is taken to be May 23, 2000, because the particulars of the instant

claims are not supported nor enabled at the locations pointed out within the meaning of 35 USC 112, first paragraph, by the parent specification as is required in order to receive the benefit of priority, essentially for reason of record. The specification of the parent application indicates that some type of adaptive mutation might be sought, but does not actually describe any adaptive mutations and does not describe or disclose the HCV NS5A variants as now claimed.

The objection to the specification as not containing a specific reference to an earlier parent application and its current status in the first sentence as set out in the prior Office action at page 4 has not been addressed and the objection is maintained.

The objection to the specification as containing hyperlinks and/or other forms of browser-executable code at page 2, line 19, of the disclosure as out in the prior Office action at pages 4-5 has not been addressed and is maintained.

The provisional obviousness type double patenting rejection over claims 95-97 of copending 09/917563 as set forth in the last Office action is withdrawn in view of Applicant's remarks.

Claim rejections under 35 USC 112, second paragraph, as previously set forth are withdrawn in light of Applicant's amendments to the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claim 9 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in Paper No. 13 filed April 10, 2002. In that paper, applicant has stated at page 5, "The invention is not directed to mutations that cause the polynucleotide to have attenuated virulence, as indicated by the amendment to claim 1," and this statement indicates that the invention is different from what is defined in the claim(s) because claim 9 recites viral properties that correspond to attenuated virulence.

Claim 1 is objected to because of the following informalities:

In the clean copy of claim 1 presented in Paper No. 13, at line 6, "at least on polyprotein" should read "at least one polyprotein."

Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9, 29, 61, 62, 69, 70, and 72-75 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for a polynucleotide comprising a non-naturally occurring HCV sequence capable of production in a host cell that comprises an adaptive mutation of the NS5A gene that confers improved cell culture characteristics to the polynucleotide, does not reasonably provide enablement for a polynucleotide comprising a non-naturally occurring HCV sequence comprising an adaptive mutation other than a mutation of the NS5A gene, for reasons of record.

Applicant has argued that Yanagi fails to teach mutations that confer improved cell culture characteristics, as the description is focused on infectious DNA clone, and speculates that mutations could be located in the P7, NS4B, and NS5A genes. Applicant cites documents by Lundkvist et al.; Frolov et al.; and Jansen et al. as showing that the state of the art indicated that adaptive viral mutations can be obtained. Applicant asserts that the specification identifies adaptive mutations in NS5A, NS3 and NS4B regions, and that other researchers, viz., Krieger et al. and Lohmann et al., have subsequently used Applicant's methods to identify adaptive mutations in other regions.

First, it is noted that the information disclosure statement filed April 4, 2002, citing the documents upon which Applicant relies in support of arguments, fails to comply with 37 CFR 1.97(c) because it lacks the fee set forth in 37 CFR 1.17(p). It has been placed in the application file, and the information referred to therein has been considered only to the extent that it relates to Applicant's remarks. The entries have been lined through to indicate that these documents will not be cited on the face of any patent that issues from the instant application.

Further, Applicant's arguments have been considered but not found persuasive. It is agreed that Yanagi only speculates where adaptive mutations might be found; this speculation has been relied upon to support the Examiner's position that the location of such mutations is unpredictable. Review of the documents of Lundkvist et al.; Frolov et al.; and Jansen et al. indicates that each type of virus tends to accumulate cell culture-adapted mutations in a region that is characteristic to that particular virus and is not seen to provide any support for predictability for locating cell culture-adaptive mutations

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in HCV. Krieger et al. disclose that host cell properties may also be important in determining replication level, further supporting the unpredictability of HCV with cell culture adaptive mutations (see, e.g., Krieger, page 4615); further, Krieger found that the most likely adaptive mutation involved NS5A, just as Applicant has found. In order to obtain additional types of mutations, Lohmann et al. apparently found it necessary to use methods for selection that go beyond what Applicant has disclosed (see, e.g., Lohmann et al., Discussion, pages 1445-1447, especially the paragraph bridging col. 1-col. 2 on page 1445). While it is so that Applicant describes clones with mutations in NS3 and NS4B, in each case these mutations do not exist alone but are found in addition to a mutation in NS5A.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 7, 9-11, 61, 62, 69, 70, and 72-74 are rejected under 35 U.S.C. 102(e) as being anticipated by Yanagi et al. for reasons of record.

Claims 3-6 and 29 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yanagi et al. for reasons of record.

Claims 8 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagi et al. in View of Mizuno et al. for reasons of record.

Applicant has argued that Yanagi makes a suggestion to try to produce HCV mutated polynucleotides, does not teach improved cell culture characteristics, does not mention any specific mutations or tell where they should be made.

These arguments have been considered but not found persuasive, since Yanagi teaches deletion of all or part of one or more regions in order to determine viral replication, which is not seen to require any methods other than those known in the art; determining viral replication in vitro, as disclosed, encompasses improved replication in cell culture, and Applicant has presented no evidence that polynucleotides disclosed by Yanagi would not have the claimed properties. Further, since the rejected claims are not drawn to any specific mutations, Applicant is relying on limitations not found in the rejected claims. Lastly, at least claim 9 presently reads on attenuating mutations.

Claims 12-17 are free of the prior art. Yanagi does not teach or fairly suggest where in NS5A a mutation or deletion should be made in order to obtain the claimed polynucleotides.

This application contains claims 18-24, 41-44, and 63-68 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must



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include cancelation of nonelected claims or other appropriate action (37 CFR 1.144)

See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:30-5:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Donna C. Wortman, Ph.D.  
Primary Examiner  
Art Unit 1648

dcw  
November 29, 2002